14:31.

U.S. Patent Appl. No. 09/963,521-Ziegler et al.

#### III. REMARKS

### Preliminary Remarks

Reconsideration and allowance of the present application based upon the foregoing amendment and following remarks are respectfully requested. Claims 19-60 are currently pending in the application. Claims 29, 38, 50, and 59 are currently objected. Claims 19-28, 30-37, 39-49, 51-58, and 60 are at issue. This response is timely filed. The applicants request entry of the foregoing amendment, as it will either place the application for allowance or place the application in better form for an appeal.

In paragraph one of the official action, the examiner objected to claims 24, 25, 31-34, 45, 46, and 52-55 for the recitation of the phrases "wherein the Corynebacterium," "wherein the Brevibacterium," and "wherein the coryneform bacteria" because these phrases allegedly lacked clarity and consistency. The applicants have amended claims 24, 25, 31-34, 45, 46, and 52-55 to recite "wherein Corynebacterium," "wherein Brevibacterium," or "wherein coryneform bacteria" where appropriate and thank the examiner for her suggestions. In view of the foregoing amendment, the applicants respectfully submit that the objection has been overcome and should be withdrawn.

In paragraph two of the official action, the examiner objected to the phrase "support page 12, line 23, 24" in claims 26 and 47. The applicants have amended claims 26 and 47 for typographical errors and not for any reasons related to patentability. In view of the foregoing amendment, the applicants respectfully submit that the objection has been overcome and should be withdrawn.

In paragraph three of the official action, the examiner objected to the phrase "wherein said coryneform bacteria also overexpress by..." in claims 27-30, 35, 36, 48-51, 56, and 57 for allegedly lacking clarity and consistency with language commonly used in the art. In paragraph four of the official action, claim 56 was further objected to for the recitation of the work "liniking" in step (a).

Amended claim 27 is now directed to the process of claim 26, wherein the Corynebacterium glutamicum pyc gene encoding pyruvate carboxylase is also overexpressed in said coryneform bacteria by increasing the copy number of said gene. Amended claim 28 is now directed to the process of claim 26, wherein the Corynebacterium glutamicum hom gene encoding homoserine dehydrogenase is also overexpressed in said coryneform bacteria by increasing the copy number of said gene. Amended claim 29 is now directed to the process of claim 26, wherein the Corynebacterium glutamicum hom<sup>dr</sup> allele encoding a

U.S. Patent Appl. No. 09/963,521-Ziegler et al.

feedback-resistant homoserine dehydrogenase is also overexpressed in said coryneform bacteria by increasing the copy number of said gene. Amended claim 30 is now directed to the process of claim 26, wherein the *Corynebacterium glutamicum mqo* gene encoding malate:quinone oxidoreductase is also overexpressed in said coryneform bacteria by increasing the copy number of said gene.

Solely to expedite prosecution, and without prejudice to seeking broader claims in a continuing application, the applicants have canceled claims 35 and 36 without prejudice. Amended claims 48-51 are directed to the process of claim 47, wherein the *Corynebacterium glutamicum pyc* gene encoding pyruvate carboxylase or *hom* gene encoding homoserine dehydrogenase, or the *hom*<sup>dr</sup> allele encoding a feedback-resistant homoserine dehydrogenase or mqo gene encoding malate:quinone oxidoreductase is also overexpressed in said coryneform bacteria by operatively linking said gene to a promoter.

Amended claim 56 is directed to a process for the fermentative preparation of Lthreonine comprising (a) fermenting L-threonine producing Corynebacterium or Brevibacterium bacteria in which a thrE gene encoding a threonine export carrier protein is overexpressed by operatively linking said gene to a promoter; and, wherein one or more of the coryneform genes selected from the group consisting of: the Corynebacterium glutamicum pyc gene encoding pyruvate carboxylase, the Corynebacterium glutamicum hom gene encoding for homoserine dehydrogenase, the Corynebacterium glutamicum hom<sup>dr</sup> allele encoding a feedback-resistant homoserine dehydrogenase, and the Corynebacterium glutamicum mqo gene encoding for malate:quinone oxidoreductase are overexpressed by operatively linking said genes to a promoter; (b) concentrating the L-threonine in the fermentation medium or in said coryneform bacteria; and (c) isolating L-threonine from the fermentation medium or coryneform bacteria of step (b). Amended claim 57 is now directed to a process for the fermentative preparation of L-threonine comprising: (a) fermenting Lthreonine producing coryneform bacteria in which a thrE gene encoding a threonine export carrier protein is overexpressed by operatively linking said gene to a promoter, and, wherein one or more of the coryneform genes selected from the group consisting of: the Corynebacterium glutamicum pyc gene encoding pyruvate carboxylase, the Corynebacterium glutamicum hom gene encoding for homoserine dehydrogenase, the Corynebacterium glutamicum hom<sup>dr</sup> allele encoding a feedback-resistant homoserine dehydrogenase, and the Corynebacterium glutamicum mqo gene encoding for malate:quinone oxidoreductase are overexpressed by operatively linking said genes to a promoter; (b) concentrating the Lthreonine in the fermentation medium or in said coryneform bacteria; and (c) isolating L-

11-22-04

threonine from the fermentation medium or coryneform bacteria of step (b) wherein said coryneform bacteria have been transformed with a plasmid vector comprising the C. glutamicum thrE gene encoding said threonine export carrier protein and said plasmid vector is pZ1thrE, which is deposited in Brevibacterium flavum under deposit number DSM12840. The applicants submit that the amendment to the claims both clarify and are consistent with the language commonly used in the art and are grateful for the examiner's suggestions. In view of the foregoing amendment and remarks, the applicants submit that the objections of paragraphs 3 and 4 have been overcome and should be withdrawn.

The applicants do not intend by these or any amendments to abandon subject matter of the claims as originally filed or later presented, and reserve the right to pursue such subject matter in continuing applications.

## Patentability Remarks

## Rejection Pursuant to 35 U.S.C. §112, Second Paragraph

In paragraph 6 of the official action, claims 20-23, 39, 41-44, and 60 were rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite. Specifically, the examiner alleged claims 20-23 and 41-44 were indefinite for the recitation of the phrases "wherein said Corynebacterium or Brevibacterium also are overexpressed by" or "wherein said coryneform bacteria also overexpress by." The examiner further asserted that these phrases were unclear because polynucleotides, not bacteria, are expressed or overexpressed. The examiner also asserted that the phrase "wherein said thrE gene comprises SEQ ID NO: 1 and SEQ ID NO: 3" is unclear as to how the thrE gene can comprise both sequences SEQ ID NOS: 1 and 3.

Amended claims 20-23 are now directed to the process of claim 19, wherein the Corynbacterium glutamicum pyc gene encoding pyruvate carboxylase or the hom gene encoding homoserine dehydrogenase or the hom<sup>dr</sup> allele encoding a feedback-resistant homoserine dehydrogenase or the mqo gene encoding malate:quinone oxidoreductase is also overexpressed in said Corynebacterium or Brevibacterium by increasing the copy number of said gene. As suggested by the examiner and for which the applicants are grateful, claims 20-23 have been amended to clarify that the pyc, hom, or hom<sup>dr</sup> genes is overexpressed by increasing the copy number of said gene in the claimed process.

U.S. Patent Appl. No. 09/963,521-Ziegler et al.

Amended claims 41-44 are now directed to the process of claim 40, wherein the Corynebacterium glutamicum pyc gene encoding pyruvate carboxylase or the hom gene encoding homoserine dehydrogenase or the hom<sup>dr</sup> allele encoding a feedback-resistant homoserine dehydrogenase or the mqo gene encoding malate:quinone oxidoreductase is also overexpressed in said Corynebacterium or Brevibacterium by operatively linking said gene to a promoter. As suggested by the examiner and for which the applicants are grateful, claims 41-44 have been amended to clarify that the pyc, hom, hom<sup>dr</sup> or mqo gene is overexpressed by operatively linking said gene to a promoter in the claimed process.

As suggested by the examiner, claims 39 and 60 have been amended to recite "wherein said thrE gene comprises SEQ ID NO: 1 or SEQ ID NO: 3" to clarify the strain origin of the thrE gene sequence from C. glutamicum. In view of the foregoing amendment and remarks, the applicants respectfully submit that the rejection of claims 20-23, 39, 41-44, and 60 under 35 U.S.C. §112, second paragraph, for allegedly being indefinite, has been overcome and should be withdrawn.

## Rejection Pursuant to 35 U.S.C. §112, First Paragraph

## Written Description

In paragraphs 10-13 of the official action, the examiner rejected claims 35 and 56 under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the written description requirement. Specifically, the examiner alleged that claims 35 and 56 lack a limitation with regard to the source of the *thr*E gene and thus the claims encompass practicing a claimed method with any gene encoding a threonine export carrier protein.

The applicants have amended claims 35 and 56 to specifically indicate that the *thrE* gene is isolated from *C. glutamicum*, which is acknowledged by the examiner as fully supported by the specification. In view of the foregoing amendment, the rejection of claims 35 and 56 under 35 U.S.C. §112, first paragraph, for allegedly lacking written description, has been overcome and should be withdrawn.

#### Enablement

In paragraph 14-17 of the official action, the examiner rejected claims 35 and 56 under 35 U.S.C. §112, first paragraph, for allegedly lacking enablement. Specifically, the examiner asserted that there is no limitation with regard to the source of the gene encoding the threonine export carrier protein in claims 35 and 56. The examiner further asserted that

14:33 -

U.S. Patent Appl. No. 09/963,521-Ziegler et al.

the claims thus encompass practicing the claimed method with any gene encoding a threonine export carrier protein.

The applicants have amended claims 35 and 56 to specifically indicate that the thrE gene is isolated from C. glutamicum, which is acknowledged by the examiner as fully enabled by the specification. In view of the foregoing amendment, the rejection of claims 35 and 56 under 35 U.S.C. §112, first paragraph, for allegedly lacking enablement, has been overcome and should be withdrawn.

# Rejection Pursuant Judicially Created Doctrine of Obviousness-Type Double Patenting

In paragraphs 18-21 of the official action, the examiner rejected claims 19-21, 23-28, 30-37, 40-42, 44-49, and 51-58 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 6 of U.S. Patent No. 6,596,516. The examiner asserted that the applicants arguments regarding the double patenting rejection were unpersuasive because the claims in the instant application do not exclude the attenuation of the glyA gene. Specifically, the examiner alleged that claim 6 of the '516 patent is more limited as it also requires the attenuation of the glyA gene. The examiner further asserted that the claims in the instant application are deemed generic, as they do not exclude the attenuation of other genes or even the overexpression of additional genes not recited in the claims. The examiner alleged that the combination of attenuating the glyA gene and overexpressing one or more genes selected from the group consisting of the thrE gene, pyc gene, mqo gene, and homA gene render the claims invention obvious.

With respect to the obviousness double patenting rejection over claim 6 of U.S. Patent No. 6,596,516, the applicants hereby enclose a terminal disclaimer, executed by the undersigned on behalf of the applicants. In view of the foregoing comments and submitted terminal disclaimer, the applicants respectfully submit that the rejection of claims 19-21, 23-28, 30-37, 40-42, 4-49, and 51-58 under the non-statutory obviousness double patenting has been overcome and should be withdrawn.

U.S. Patent Appl. No. 09/963,521-Ziegler et al.

## IV. CONCLUSION

In view of the foregoing, the claims are now believed to be in form of allowance, and such action is hereby solicited. If any point remains at issue which the examiner feels may be best resolved through a personal or telephone interview, please contact the undersigned at the telephone number below.

Respectfully submitted,

PILLSBURY WINTHROP LLP

Thomas A. Cawley, Jr., Ph.D.

Reg. No. 40,944

Tel. No. (703) 905-2144 Fax No. (703) 905-2500

November 22, 2004 TAC/PAJ P.O. Box 10500 McLean, VA 22102 (703) 905-2000